

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

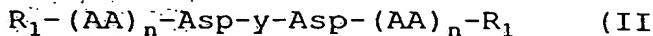
- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

What Is Claimed Is:

1. A reporter compound having the general Formula II:



5

or a biologically acceptable salt or pro-reporter molecule thereof, wherein

R₁ is an N-terminal protecting group;

each AA independently is a residue of an α-amino acid or β-amino acid, or a derivative of an α-amino acid or β-amino acid;

10

each n independently is 0-5; and

y is a fluorogenic or fluorescent moiety.

2. The compound of claim 1 wherein R₁-(AA)_n-Asp is an N-blocked tetrapeptide which is a substrate for a caspase enzyme.

15

3. The compound of claim 2, wherein said tetrapeptide is WEHD SEQ ID NO:1, YVAD SEQ ID NO:2, LEHD SEQ ID NO:3, DETD SEQ ID NO:4, DEVD SEQ ID NO:5, DEHD SEQ ID NO:6, VEHD SEQ ID NO:7, LETD SEQ ID NO:8, LEHD SEQ ID NO:3, SHVD SEQ ID NO:10, DELD SEQ ID NO:11, DGPD SEQ ID NO:12, DEPD SEQ ID NO:13, DGTD SEQ ID NO:14, DLND SEQ ID NO:15, DEED SEQ ID NO:16, DSDL SEQ ID NO:17, DVPD SEQ ID NO:18, DEAD SEQ ID NO:19, DSYD SEQ ID NO:20, ELPD SEQ ID NO:21, VEID SEQ ID NO:26 or IETD SEQ ID NO:24.

20

25

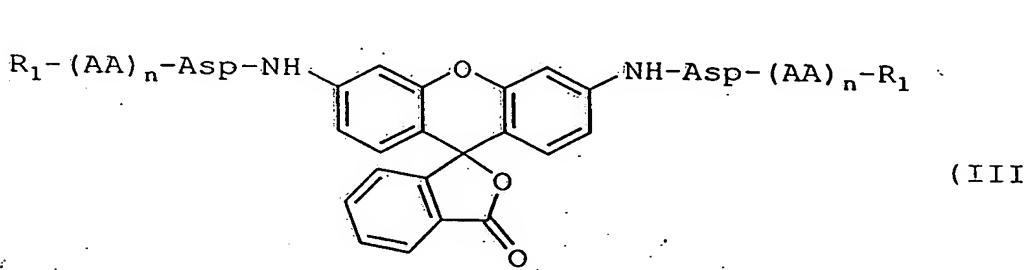
4. The compound of claim 1, wherein R₁-(AA)_n-Asp is an N-blocked tetrapeptide which is a substrate for granzyme B.

5. The compound of claim 4, wherein R₁-(AA)_n-Asp is IEPD or VEPD.

6. The compound of claim 1, wherein R₁-(AA)_n-Asp is an N-blocked peptide consisting of C-terminal Asp and 1, 2 or 3 amino acids of a peptide chain selected from the group consisting of WEHD SEQ ID NO:1, YVAD SEQ ID NO:2, LEHD SEQ ID NO:3, DETD SEQ ID NO:4, DEVD SEQ ID NO:5, DEHD SEQ ID NO:6, VEHD SEQ ID NO:7, LETD SEQ ID NO:8, LEHD SEQ ID NO:9, SHVD SEQ ID NO:10, DELD SEQ ID NO:11, DGPD SEQ ID NO:12, DEPD SEQ ID NO:13, DGTD SEQ ID NO:14, DLND SEQ ID NO:15, DEED SEQ ID NO:16, DSDL SEQ ID NO:17, DVVPD SEQ ID NO:18, DEAD SEQ ID NO:19, DSYD SEQ ID NO:20, ELPD SEQ ID NO:21, VEID SEQ ID NO:26, IETD SEQ ID NO:24, IEPD SEQ ID NO:23 and VEPD SEQ ID NO:27.

15. The compound of claim 1, wherein y is Rhodamine 110; and the pro-reporter molecule is a lower alkyl ester or an acetoxyethyl (AM) ester of an Asp- or Glu-containing compound.

20. The compound of claim 1, having the formula III:



25. The compound of claim 8, wherein R₁ is t-butyloxycarbonyl, acetyl, hexanoyl, octanoyl or benzyloxycarbonyl.

10. The compound of claim 8, wherein -(AA)_n is WEH, YVA, LEH, DET, DEV, DEH, VEH, LET, SHV, DEL, DGP, DEP, DGT, DLN, DEE, DSL, DVP, DEA, DSY, ELP, VED, IEP or IET.

5 11. The compound of claim 1, which is selected from the group consisting of

(Z-YVAD)₂-Rhodamine 110, SEQ ID NO:2;

(Z-DEVD)₂-Rhodamine 110, SEQ ID NO:5;

(Z-VAD)₂-Rhodamine 110;

10 (Z-YVAD(OAM))₂-Rhodamine 110, SEQ ID NO:2;

(Z-LE(OAM)HD(OAM))₂-Rhodamine 110, SEQ ID NO:3;

(Z-D(OAM)E(OAM)TD(OAM))₂-Rhodamine 110, SEQ ID NO:4;

(Z-D(OAM)E(OAM)VD(OAM))₂-Rhodamine 110, SEQ ID NO:5;

15 (Z-D(OMe)E(OMe)VD(OAM))₂-Rhodamine 110, SEQ ID NO:5; and

(Z-D(OMe)E(OMe)VD)₂-Rhodamine 110 SEQ ID NO:5.

12. A method for the preparation of a compound of claim 8, comprising

20 (a) condensing Rhodamine 110 together with *N*-fmoc-L-aspartic acid β -*t*-butyl ester to give (Fmoc-Asp(OBu-t))₂-Rhodamine 110;

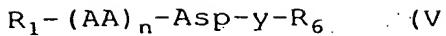
(b) removing the Fmoc group to give (Asp(OBu-t))₂-Rhodamine 110;

25 (c) condensing (Asp(OBu-t))₂-Rhodamine with Z-(AA)_n to give (Z-(AA)_n-Asp(OBu-t))₂-Rhodamine 110; and

(d) removing the OBu-t protecting group.

13. The method of claim 12, wherein -(AA)_n is WEH, YVA, LEH, DET, DEV, DEH, VEH, LET, SHV, DEL, DGP, DEP, DGT, DLN, DEE, DSL, DVP, DEA, DSY, ELP, VED, IEP or IET.

30 14. A reporter compound having the general Formula V:



or a biologically acceptable salt or pro-reporter molecule thereof, wherein
5 R_1 is an *N*-terminal protecting group;

R_6 is a blocking group which is not an amino acid or a derivative of an amino acid;

each AA independently is a residue of an α -amino acid or β -amino acid, or a derivative of an α -amino acid or β -amino acid;

n is 0-5; and

10 y is a fluorogenic or fluorescent moiety.

15. The compound of claim 14 wherein $R_1-(AA)_n-Asp$ is an *N*-blocked tetrapeptide which is a substrate for a caspase enzyme.

16. The compound of claim 15, wherein said tetrapeptide is WEHD SEQ ID NO:1, YVAD SEQ ID NO:2, LEHD SEQ ID NO:3, DETD SEQ ID NO:4, DEVD SEQ ID NO:5, DEHD SEQ ID NO:6, VEHD SEQ ID NO:7, LETD SEQ ID NO:8, LEHD SEQ ID NO:3, SHVD SEQ ID NO:10, DELD SEQ ID NO:11, DGPD SEQ ID NO:12, DEPD SEQ ID NO:13, DGTD SEQ ID NO:14, DLND SEQ ID NO:15, DEED SEQ ID NO:16, DSLD SEQ ID NO:17, DVPD SEQ ID NO:18, DEAD SEQ ID NO:19, DSYD SEQ ID NO:20, ELPD SEQ ID NO:21, VEID SEQ ID NO:26 or IETD SEQ ID NO:24.

20. The compound of claim 14, wherein $R_1-(AA)_n-Asp$ is an *N*-blocked tetrapeptide which is a substrate for granzyme B.

25. The compound of claim 17, wherein $R_1-(AA)_n-Asp$ is *N*-blocked IEPD or VEPD.

5 19. The compound of claim 14, wherein R₁-(AA)_n-Asp is an N-blocked peptide consisting of C-terminal Asp and 1, 2 or 3 amino acids of a peptide chain selected from the group consisting of WEHD SEQ ID NO:1, YVAD SEQ ID NO:2, LEHD SEQ ID NO:3, DETD SEQ ID NO:4, DEVD SEQ ID NO:5, DEHD SEQ ID NO:6, VEHD SEQ ID NO:7, LETD SEQ ID NO:8, LEHD SEQ ID NO:9, LEVD SEQ ID NO:10, SHVD SEQ ID NO:11, DELD SEQ ID NO:12, DGPD SEQ ID NO:13, DEPD SEQ ID NO:14, DLND SEQ ID NO:15, DEED SEQ ID NO:16, DSDL SEQ ID NO:17, DVPD SEQ ID NO:18, DEAD SEQ ID NO:19, DSYD SEQ ID NO:20, ELPD SEQ ID NO:21, VEID SEQ ID NO:22 or IETD SEQ ID NO:23, IEPD SEQ ID NO:24 and VEPD SEQ ID NO:25.

10

15 20. The compound of claim 14, wherein y is Rhodamine 110.

21. The compound of claim 14, wherein R₆ is CH₃OCO-, Cbz, Cl₃CCH₂OCO-, PhCH₂CH₂OCO-, or CH₃(CH₂)_pOCO-, where p is 1-11.

20 22. The compound of claim 14, wherein R₆ is Me₂NCO-, Et₂NCO-, or N-Me-N-CH₃(CH₂)_vNCO-, where v is 0-9.

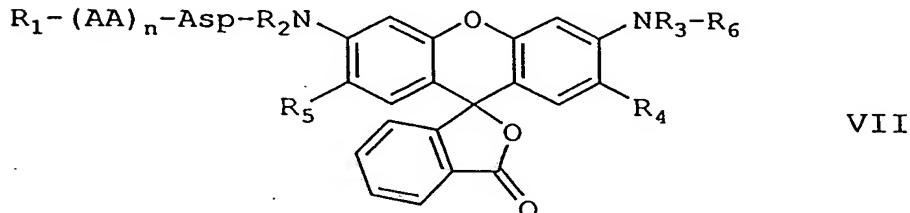
25 23.. The compound of claim 14, wherein R₆ is Ts-, PhSO₂-, MeSO₂, PhCH₂SO₂-, CF₃SO₂- or CH₃(CH₂)_uSO₂-, where u is 0-11.

24. The compound of claim 14, wherein R₆ is CH₃SCO-, or CH₃(CH₂)_tSCO-, where t is 0-11.

30 25. The compound of claim 14, wherein R₆ is HCO-, CH₃CO-, PhCH₂CO-, PhCO- or CH₃(CH₂)_wCO-, where w is 0-11.

26. The compound of claim 14, wherein R₆ is CH₃(OCH₂CH₂)_qOCO-, or CH₃(CH₂)_r(OCH₂CH₂)_sOCO-, where q is 1-4, r is 0-5 and s is 1-4.

27. The compound of claim 14, having the formula VII:



10 or a biologically acceptable salt or pro-reporter molecule thereof, wherein R₂ and R₃ independently are hydrogen, methyl or ethyl; and R₄ and R₅ independently are hydrogen or methyl.

15 28. The compound of claim 27, wherein R₁ is t-butyloxycarbonyl, acetyl, hexanoyl, octanoyl or benzyloxycarbonyl; and R₂, R₃, R₄ and R₅ are hydrogen.

20 29. The compound of claim 27, wherein -(AA)_n is WEH, YVA, LEH, DET, DEV, DEH, VEH, LET, LEV, SHV, DEL, DGP, DEP, DGT, DLN, DEE, DSL, DVP, DEA, DSY, ELP, VED, IEP or IET.

25 30. The compound of claim 14, which is selected from the group consisting of

N-(Z-YVAD)-N'-acetyl-Rhodamine 110, SEQ ID NO:2;

N-(Z-DEVD)-N'-acetyl-Rhodamine 110, SEQ ID NO:5;

N-(Z-VD)-N'-acetyl-Rhodamine 110;

N-(Z-AD)-N'-acetyl-Rhodamine 110;

N-(Z-VAD)-N'-acetyl-Rhodamine 110;

N-(Z-DEVD)-N'-ethoxycarbonyl-Rhodamine 110, SEQ ID NO:5;

N-(Ac-DEVD)-*N'*-ethoxycarbonyl-Rhodamine 110, SEQ ID NO:5;
N-(Ac-DEVD)-*N'*-hexyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;
N-(Ac-DEVD)-*N'*-octyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;
N-(Ac-DEVD)-*N'*-decyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;
N-(Ac-DEVD)-*N'*-dodecyloxycarbonyl-Rhodamine 110, SEQ ID NO:5;

5 and

N-(Ac-DEVD)-*N'*-(ethylthio)carbonyl-Rhodamine 110, SEQ ID NO:5.

31. A method for the preparation of a compound of claim 27,
comprising

10 (a) reacting Rhodamine with acetic anhydride to give *N*-acetyl-Rhodamine;

(b) condensing *N*-acetyl-Rhodamine together with *N*-fmoc-L-aspartic acid β -*t*-butyl ester to give *N*-(Fmoc-Asp(OBu-t))-*N'*-acetyl-Rhodamine;

15 (c) removing the Fmoc group to give *N*-(Asp(OBu-t))-*N'*-acetyl-Rhodamine;

(d) condensing *N*-(Asp(OBu-t))-*N'*-acetyl-Rhodamine with *Z*-(AA)_n to give *N*-(*Z*-(AA)_n-Asp(OBu-t))-*N'*-acetyl-Rhodamine; and

(e) removing the OBu-t protecting group to give *N*-(*Z*-(AA)_n-Asp)-*N'*-acetyl-Rhodamine.

20 32. A method for the preparation of a compound of claim 27,
comprising

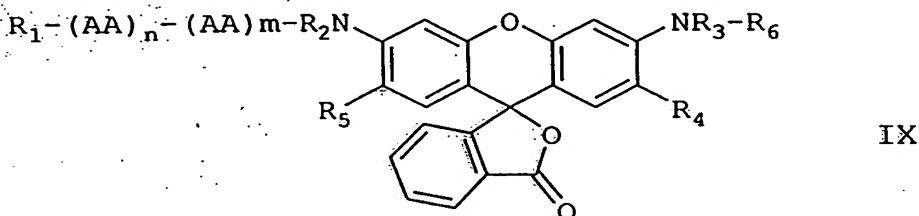
(a) reacting Rhodamine with acetic anhydride to give *N*-acetyl-Rhodamine;

25 (b) condensing *N*-acetyl-Rhodamine with *Z*-(AA)_n-Asp(OBu-t) to give *N*-(*Z*-(AA)_n-Asp(OBu-t))-*N'*-acetyl-Rhodamine; and

(c) removing the OBu-t protecting group to give *N*-(*Z*-(AA)_n-Asp)-*N'*-acetyl-Rhodamine.

33. The method of claim 31 or 32, wherein -(AA)_n is WEH, YVA, LEH, DET, DEV, DEH, VEH, LET, LEV, SHV, DEL, DGP, DEP, DGT, DLN, DEE, DSL, DVP, DEA, DSY, ELP, VED, IEP or IET.

5 34. The compound of claim 1, having the formula IX:



or a biologically acceptable salt or pro-reporter molecule thereof, wherein
R₁ is a hydrogen or a N-terminal protecting group;
10 R₆ is a blocking group which is not an amino acid or a derivative of an amino acid;
each AA independently is a residue of an α -amino acid or β -amino acid, or a derivative of an α -amino acid or β -amino acid;
n is an integer of 0-5;
15 m is an integer of 0-3;
R₂ and R₃ independently are hydrogen, methyl or ethyl; and
R₄ and R₅ independently are hydrogen or methyl.

20 35. The compound of claim 34, wherein R₂, R₃, R₄ and R₅ are hydrogen.

25 36. The compound of claim 34, wherein R₁ is H; n=1; (AA)_n is M; m is an integer from 1-2; and (AA)_m is selected from the group consisting of GG, GA, AG, G, and A.

37. The compound of claim 34, wherein the compound is selected from the group consisting of

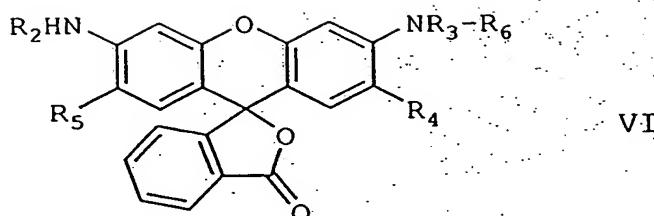
N-(GP)-*N'*-ethoxycarbonyl-Rhodamine 110,
N-(GPG)-*N'*-ethoxycarbonyl-Rhodamine 110, and
N-G-*N'*-octyloxycarbonyl-Rhodamine 110.

5 38. The compound of claim 34, wherein R₇ is a N-terminal protecting group selected from the group consisting of t-butyloxycarbonyl, acetyl, hexanoyl, octanoyl, dodecanoyl and benzyloxycarbonyl.

10 39. The compound of claim 34, wherein (AA)_n-(AA)_m is selected from the group consisting of SQNY-PIV SEQ ID NO:28, ARVL-AEA SEQ ID NO:29, ATIM-MQR SEQ ID NO:30, RQAN-FLG SEQ ID NO:31, PGNF-LQS SEQ ID NO:32, SFSF-PQI SEQ ID NO:33, TLNF-PIS SEQ ID NO:34, AETF-YVD SEQ ID NO:35 or RKVL-FLD SEQ ID NO:36; SQNY-PI SEQ ID NO:117, ARVL-AE SEQ ID NO:118, ATIM-MQ SEQ ID NO:119, RQAN-FL SEQ ID NO:120, PGNF-LQ SEQ ID NO:121, SFSF-PQ SEQ ID NO:122, TLNF-PI SEQ ID NO:123, AETF-YV SEQ ID NO:124 or RKVL-FL SEQ ID NO:125; SQNY-P SEQ ID NO:126, ARVL-A SEQ ID NO:127, ATIM-M SEQ ID NO:128, RQAN-F SEQ ID NO:129, PGNF-L SEQ ID NO:130, SFSF-P SEQ ID NO:131, TLNF-P SEQ ID NO:132, AETF-Y SEQ ID NO:133 and RKVL-F SEQ ID NO:134.

20 40. The compound of claim 34, wherein (AA)_n-(AA)_m is selected from the group consisting of LRGGG SEQ ID NO:101, LRGGA SEQ ID NO:102, MRGGG SEQ ID NO:96, MRGGA SEQ ID NO:135, IRGGG SEQ ID NO:97, IRGGA SEQ ID NO:136, LVGGG SEQ ID NO:98, LVGGA SEQ ID NO:137, MVGGG SEQ ID NO:99, MVGGA SEQ ID NO:138, IVGGG SEQ ID NO:100, IVGGA SEQ ID NO:139, LRGG SEQ ID NO:55, MRGG SEQ ID NO:56, IRGG SEQ ID NO:57, LVGG SEQ ID NO:58, MVGG SEQ ID NO:59 and IVGG SEQ ID NO:60.

30 41. A compound having the general Formula VI:



or a biologically acceptable salt thereof, wherein

5 R_2 and R_3 independently are hydrogen, methyl or ethyl;
 R_4 and R_5 independently are hydrogen or methyl;
 R_6 is a blocking group which is not an amino acid or a derivative of an amino acid.

10 42. The compound of claim 41, wherein R_2 , R_3 , R_4 and R_5 are hydrogen.

43. The compound of claim 41, wherein R_2 and R_3 are methyl; and R_4 and R_5 are hydrogen.

15 44. The compound of claim 41, wherein R_2 and R_3 are ethyl; and R_4 and R_5 are methyl.

20 45. The compound of claim 41, which is selected from the group consisting of
 N -methoxycarbonyl-Rhodamine 110,
 N -ethoxycarbonyl-Rhodamine 110,
 N -hexyloxycarbonyl-Rhodamine 110,
 N -octyloxycarbonyl-Rhodamine 110,
 N -decyloxycarbonyl-Rhodamine 110, and

N-dodecyloxycarbonyl-Rhodamine 110.

46. The compound of claim 41, which is selected from the group consisting of

5 *N*-dimethylcarbamyl-Rhodamine 110,
 N-(*N*-methyl-*N*-hexylcarbamyl)-Rhodamine 110,
 N-methanesulfonyl-Rhodamine 110,
 N-(ethylthio)carbonyl-Rhodamine 110,
 N-(hexylthio)carbonyl-Rhodamine 110,
10 *N*-(octylthio)carbonyl-Rhodamine 110,
 N-acetyl-Rhodamine 110,
 N-acetyl-Rhodamine 116,
 N-(2,5,8-trioxadecyloxycarbonyl)-Rhodamine 110 and
 N-(2-butoxyethoxycarbonyl)-Rhodamine 110.

15 47. A method for detecting an enzyme involved in the apoptosis cascade in one or more cells, comprising

20 (a) contacting said one or more cells with the reporter compound according to claim 1 or 14 under conditions whereby said reporter compound is taken into said one or more cells, and
 (b) recording the fluorescence of said one or more cells, wherein a change in fluorescence within said one or more cells compared to control cells which have not been so contacted is an indication of the presence of the enzyme.

25 48. The method of claim 47, wherein said enzyme is an intracellular caspase.

30 49. A method for measuring the activity of an enzyme involved in the apoptosis cascade in one or more cells, comprising

(a) contacting said one or more cells with the reporter compound according to claim 1 or 14 under conditions whereby said reporter compound is taken into said one or more cells, and

5 (b) recording the fluorescence of said one or more cells, wherein the relative change in fluorescence within said one or more cells compared to control cells which have not been so contacted is a measure of the activity of the enzyme.

10 50. The method of claim 49, wherein said enzyme is an intracellular caspase.

15 51. A method for determining whether a test substance has an effect on an enzyme involved in the apoptosis cascade in one or more test cells, comprising

(a) contacting said one or more test cells with said test substance and the reporter compound according to claim 1 or 14 under conditions whereby said test substance either interacts with an external receptor or is taken into said one or more cells and said reporter compound is taken into said one or more cells, and

20 (b) recording the fluorescence of said one or more test cells compared to control cells which have only been contacted with said reporter compound, wherein a change in fluorescence within said one or more test cells compared to said control cells is an indication that said test substance has an effect on said enzyme.

25 52. The method of claim 51, wherein said enzyme is an intracellular caspase.

30 53. The method according to claim 51, wherein said one or more test cells is contacted with said test substance prior to contacting said test cells with said reporter compound.

54. The method according to claim 51, wherein said one or more test
cells is contacted with said test substance after contacting with said reporter
compound.

5 55. The method according to claim 51, wherein said one or more test
cells is contacted substantially simultaneously with said test substance and said
reporter compound.

10 56. The method according to claim 51, wherein said method is to
determine whether said test substance stimulates the activity of said enzyme.

57. The method according to claim 51, wherein said method is to
determine whether said test substance inhibits the activity of said enzyme.

15 58. The method according to claim 51, wherein said contacting step
further includes contacting said one or more test cells with at least one second test
substance in the presence of said first test substance.

20 59. The method according to claim 51, wherein said one or more test
cells are derived from a single-cell organism.

60. The method according to claim 51, wherein said one or more test
cells is derived from a multi-cellular organism.

25 61. The method according to claim 60, wherein said multi-cellular
organism is selected from the group consists of a mammal, an invertebrate animal,
an insect and a plant.

30 62. The method according to claim 51, wherein the one or more test
and control cells are derived from the group consisting of the hair, brain,

5 peripheral nervous system, eye, ear, nose, mouth, tonsils, teeth, esophagus, lung, breast, heart, blood, blood vessels, bone marrow, lymph nodes, thymus, spleen, immune system, liver, stomach, intestinal tract, pancreas, endocrine glands and tissues, kidney, bladder, reproductive organs or glands, joint, bone and skin of said multicellular organism.

10 63. The method according to claim 51, wherein the one or more test cells are cancerous.

15 64. The method according to claim 63, wherein said one or more cancerous test cells are derived from the group consisting of the brain, peripheral nervous system, eye, ear, nose, mouth, tonsils, teeth, esophagus, lung, breast, heart, blood, blood vessels, bone marrow, lymph nodes, thymus, spleen, immune system, liver, stomach, intestinal tract, pancreas, endocrine glands or tissues, kidney, bladder, reproductive organs or glands, joints, bones and skin of said multi-cellular organism.

20 65. The method according to claim 63, wherein said one or more cancerous test cells are derived from a human in need of treatment with a chemotherapeutic drug and said test substance is a chemotherapeutic agent.

25 66. The method according to claim 51, wherein the test substance is a chemotherapeutic agent.

67. The method according to claim 51, wherein the test substance is a mixture of chemotherapeutic agents.

68. A method to determine the sensitivity of an animal with cancer to treatment with one or more chemotherapeutic agents, comprising

(a) contacting cancer cells taken from said animal with said one or more chemotherapeutic agents and the reporter compound according to claim 1 or 14 under conditions whereby said one or more agents, either interacts with an external receptor or is taken into said cancer cells, and

5 (b) recording the fluorescence of said cancer cells compared to control cells which have only been contacted with said reporter compound, wherein a change in fluorescence of said cancer cells compared to said control cells is an indication that said cancer cells are chemosensitive to said one or more chemotherapeutic agents and that said animal is sensitive to said treatment.

10

69. The method of claim 68, wherein said animal is a human.

70. A method for monitoring the treatment of an animal to treatment with one or more chemotherapeutic agents, comprising

15 (a) administering said one or more chemotherapeutic agents to said animal,

(b) contacting cells taken from said animal after said administering with the reporter compound according to claim 1 or 14 under conditions whereby said reporter compound is taken into said cells, and

20 (c) recording the fluorescence of said cells contacted with said reporter compound compared to control cells which have been taken from said animal before said administering,

wherein a change in fluorescence of said cells taken from said animal compared to said control cells is an indication that said animal is sensitive to said chemotherapeutic agents.

25

71. The method according to claim 70, wherein said animal suffers from a malady related to apoptotic cell death.

72. A method for determining whether a test substance inhibits or prevents cell death in one or more test cells, comprising

(a) contacting said one or more test cells with said test substance and the reporter compound according to claim 1 or 14 under conditions whereby said reporter compound is taken into said one or more cells, and

(b) recording the fluorescence of said one or more test cells compared to control cells which have only been contacted with said reporter compound, wherein a decrease in fluorescence within said one or more test cells compared to said control cells is an indication that said test substance inhibits or prevents cell death.

10 73. The method of claim 72, wherein said one or more test cells are nerve cells.

15 74. The method of claim 72, wherein said one or more test cells are selected from the group consisting of myocardial cells, immune cells, cells of an organ to be transplanted, spermatozoa, egg, cell lines which produces a recombinant protein, hair cells, skin cells and nerve cells.

20 75. A method for determining whether a test substance causes or enhances cell death in one or more test cells, comprising

(a) contacting said one or more test cells with said test substance and the reporter compound according to claim 1 or 14 under conditions whereby said reporter compound are taken into said one or more cells, and

25 (b) recording the fluorescence of said one or more test cells compared to control cells which has only been contacted with said reporter compound, wherein an increase of fluorescence within said one or more test cells compared to said control cells is an indication that said test substance causes or enhances cell death.

76. The method of claim 75, wherein said one or more test cells are cancer cells, yeast, fungi or bacteria.

5 77. A method for detecting a viral protease in one or more cells, comprising

(a) contacting said cells with the reporter compound of claim 34 under conditions whereby the reporter compound is taken into the cells, and

10 (b) recording the fluorescence of said cells, wherein a change in fluorescence within the cells compared to control cells which have not been so contacted is an indication of the presence of the viral protease.

78. A method for measuring the activity of a viral protease in one or more viral infected cells, comprising

15 (a) contacting said one or more viral infected cells with the reporter compound of claim 34 under conditions whereby the reporter compound is taken into said one or more viral infected cells, and

20 (b) recording the fluorescence of said one or more cells, wherein a change in fluorescence within said one or more viral infected cells compared to control cells which have not been so contacted is a measure of the activity of the viral protease.

79. A method for determining whether a test substance has an effect on the activity of viral protease in one or more viral infected cells, comprising

25 (a) contacting said viral infected test cells with said test substance and the reporter compound of claim 34 under conditions whereby said reporter compound is taken into said infected test cells, and

 (b) recording the fluorescence of said infected test cells compared to infected control cells which have only been contacted with said reporter compound,

wherein a change in fluorescence within said infected test cells compared to said infected control cells is an indication that said test substance has an effect, on the viral protease.

5 80. The method of any one of claims 77-79, wherein said cells are HIV infected cells and the viral protease is HIV protease.

10 81. The method of any one of claims 77-79, wherein said cells are adenovirus infected cells and the viral protease is adenovirus protease.

15 82. The method of any one of claims 77-79, wherein said cells are HSV infected cells and the viral protease is HSV protease.

20 83. The method of any one of claims 77-79, wherein said cells are HCMV infected cells and the viral protease is HCMV protease.

25 84. The method of any one of claims 77-79, wherein said cells are HCV infected cells and the viral protease is HCV protease.

30 85. A method for measuring the activity of protease or peptidase in cells, comprising

(a) contacting the test cells with the reporter compound of claim 34 under conditions whereby the reporter compound is taken into said test cells, or the reporter compound is interacting with an external membrane protease or peptidase of said cells, and

(b) recording the fluorescence of said cells,
wherein a change in fluorescence within said test cell compared to control cells which have not been so contacted is a measure of the activity of the said protease or peptidase.

86. A method for determining whether a test substance has an effect on the activity of protease or peptidase in the test cells, comprising

(a) contacting said test cells with said test substance and the reporter compound of claim 34 under conditions whereby said reporter compound is taken into said test cells, or the reporter compound is interacting with an external membrane protease or peptidase of said cells, and

(b) recording the fluorescence of said test cells compared to control cells which have only been contacted with said reporter compound, wherein a change in fluorescence within the test cells compared to said control cells is an indication that said test substance has an effect on the said protease or peptidase.

10 87. The method of any one of claims 85-86, wherein said cells are endothelial cells and the peptidase is type 2 methionine aminopeptidase.

15 88. The method of any one of claims 85-86, wherein said cells are T cells and the peptidase is dipeptidyl peptidase-IV.

20 89. The method of any one of claims 85-86, wherein said cells are neuron cells and the protease is calpain.

90. The method of any one of claims 85-86, wherein said peptidase is aminopeptidase.